Armed Forces College of Medicine

AFCM

كلية الطب بالقوات المسلحة

Armed Forces College of Medicine

Innate Immunity

(Part 1& 2)

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Intended learning objectives (ILOs) of Introduction to Immunology

By the end of this lecture the student will be able to:

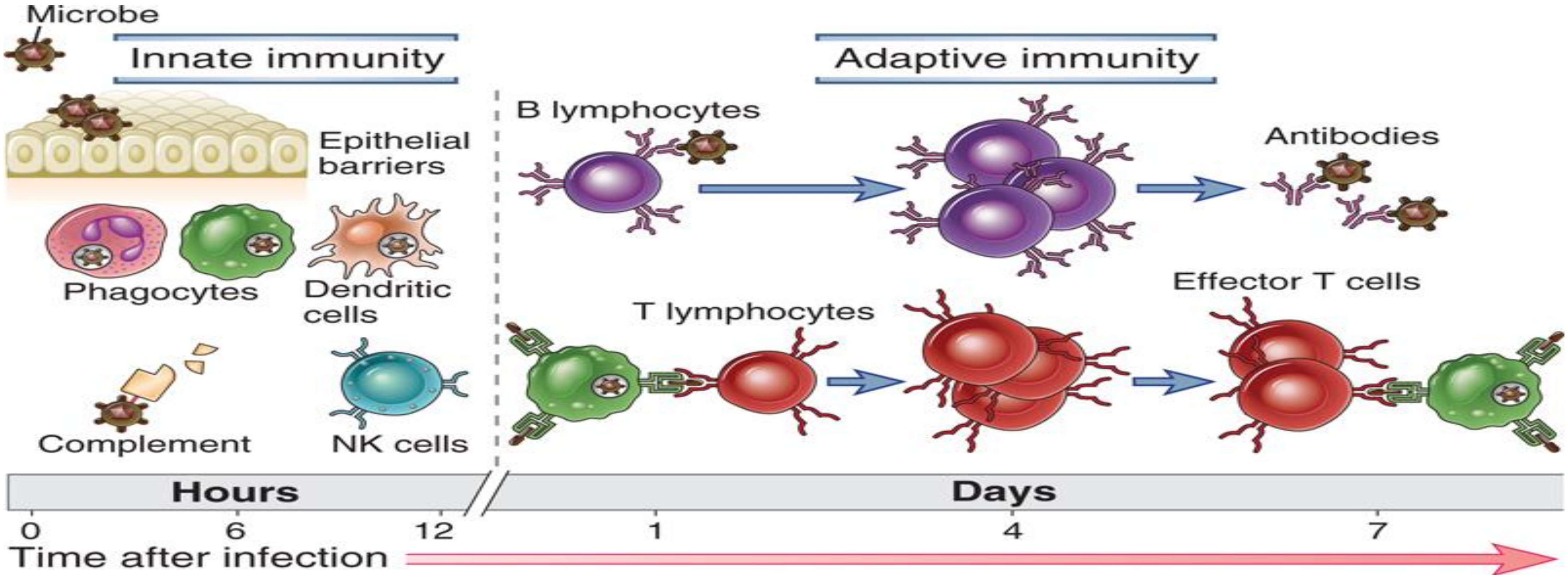
1. ***Describe functions and components of innate immunity***
2. ***Outline functions of 1ry & 2ry lymphoid organs***
3. ***Compare characters of innate immunity to those of adaptive immunity***.

Types Of Immunity

A) Innate (Natural) Immunity

1) **1st line** of defense → mediates initial protection against infection

2) **Activates adaptive immune response**



COMPONENTS & REACTIONS OF INNATE IMMUNITY

Mechanical & Chemical barriers

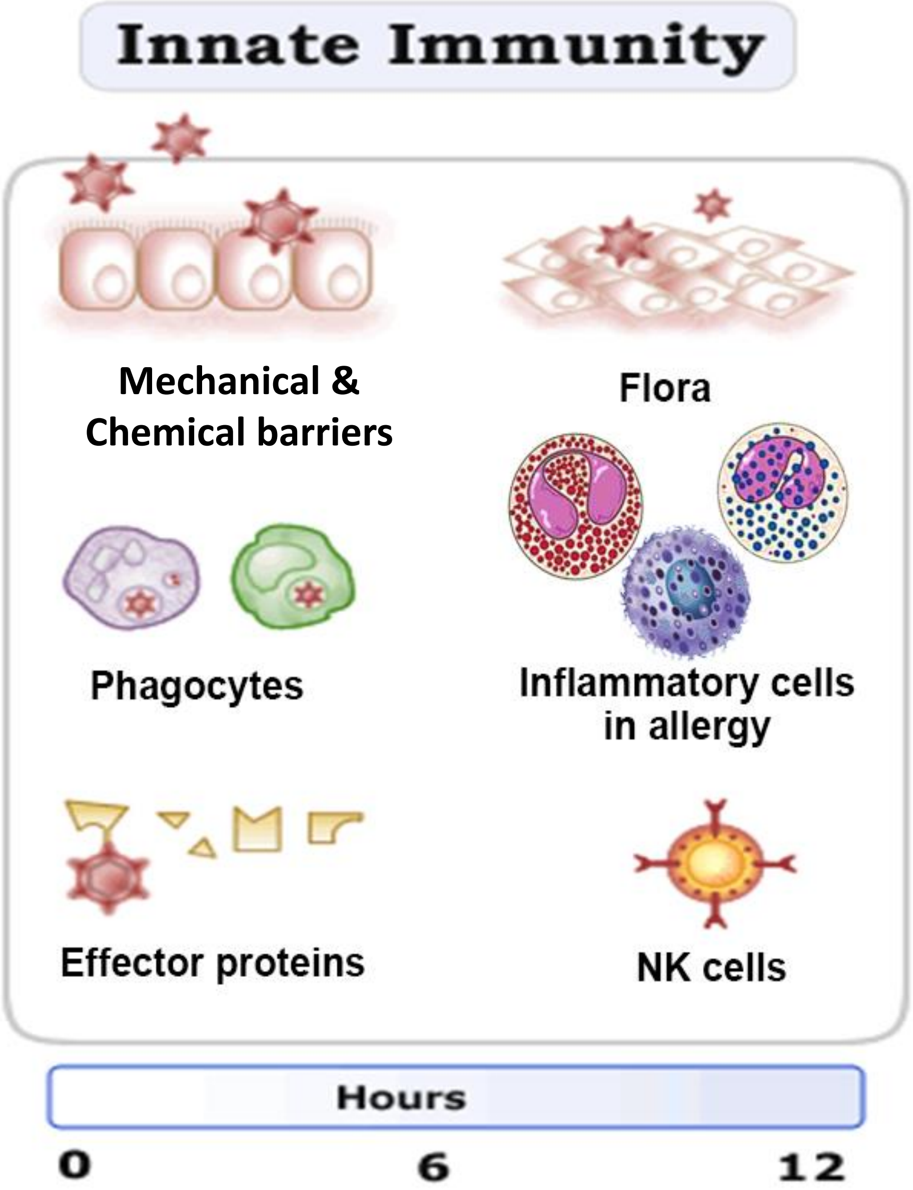
Normal Microbial flora

Phagocytes & Phagocytosis

Inflammation & Inflammatory cells involved in allergy

Circulating effector proteins

Innate lymphoid cells (NK cells)



I) Mechanical & Chemical barriers

A) Mechanical barriers

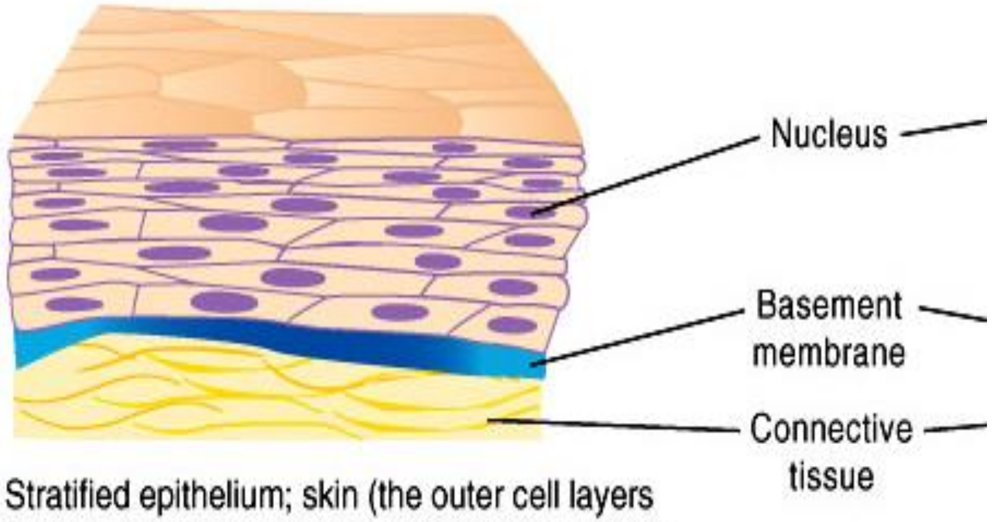
- Skin
- Mucus
- Cilia

I) Mechanical & Chemical barriers

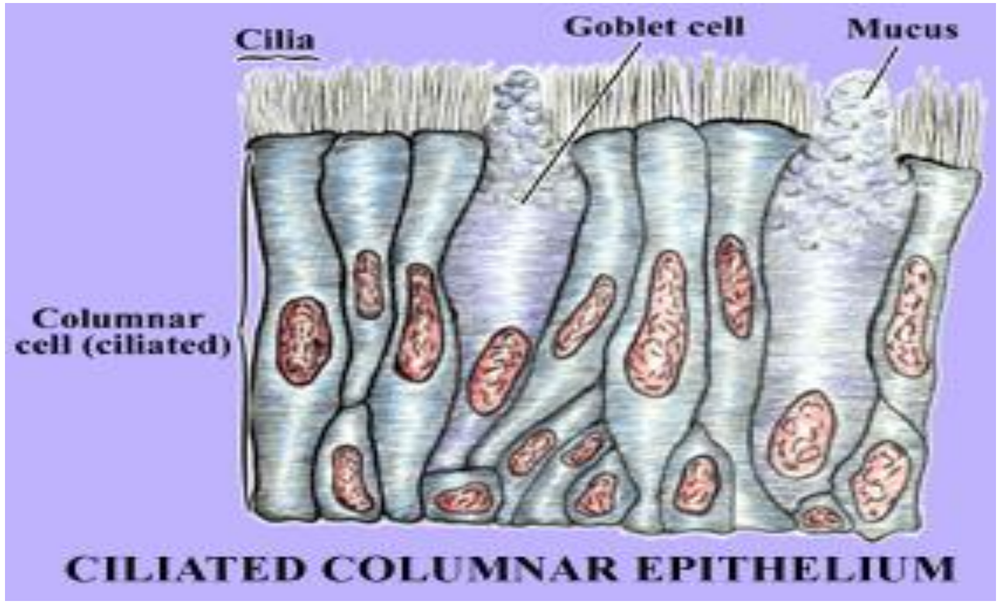
A) Mechanical barriers

Prevent attachment and / or entry of microbes

- Intact skin & epithelium of Respiratory tract (RT) and Gastrointestinal tract (GIT)
- Sticky mucus covering respiratory tract (RT) → Traps inhaled organisms
- Cilia → Sweep organisms in mucus



Stratified epithelium; skin (the outer cell layers are embedded with keratin), lining of the mouth



I) Mechanical & Chemical barriers

B) Chemical barriers

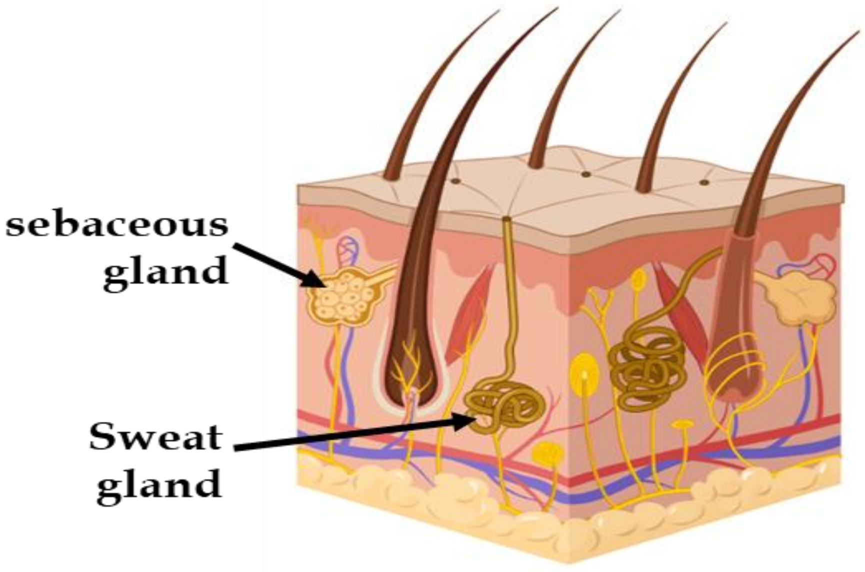
- Acids
- Lysosymes
- Defensins

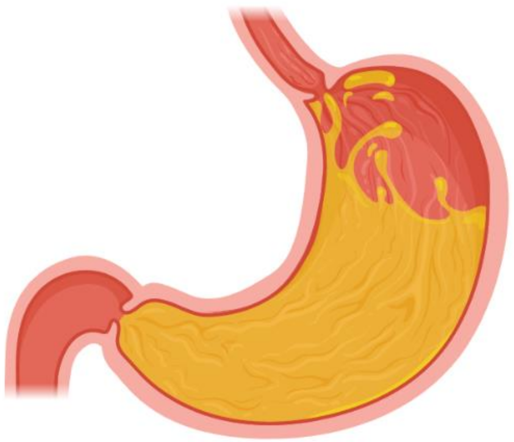
I) Mechanical & Chemical barriers

B) Chemical barriers

Kill microbes (cidal) or ⊖ their growth

1) Acids (low pH)	
Fatty & lactic acids	**HCl**
in sweat & sebaceous secretions	in gastric juice





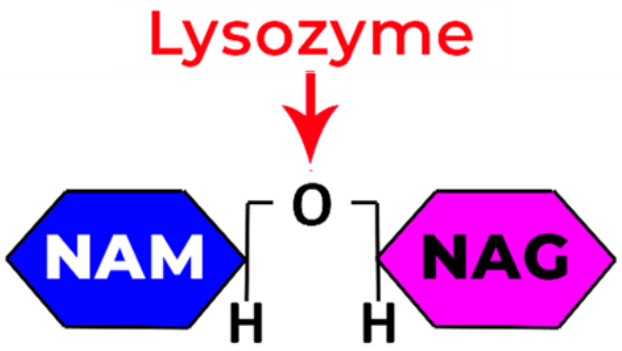
I) Mechanical & Chemical barriers

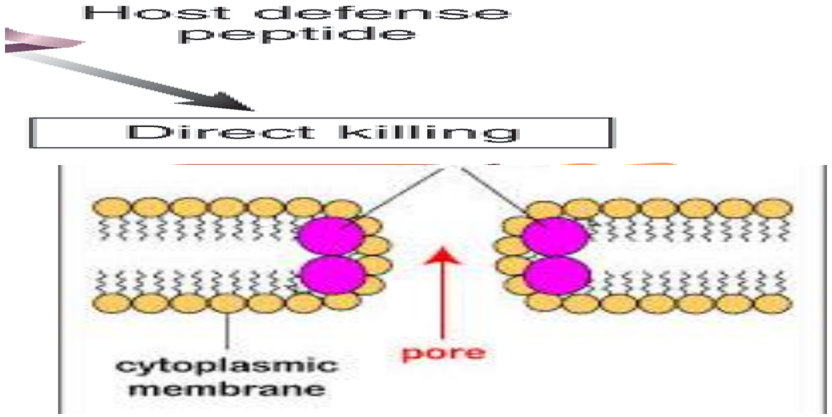
B) Chemical barriers

Kill microbes (cidal) or ⊖ their growth

2) Antimicrobial peptides

Lysosymes	Defensins
In tears, nasal secretions & saliva ↓ Degrade peptidoglycan in bacterial cell wall	- Toxic to microbes (create pores in microbial membranes)





II) Normal Microbial Flora

Cover epithelial surfaces

↓

Inhibit growth of pathogenic bacteria by:

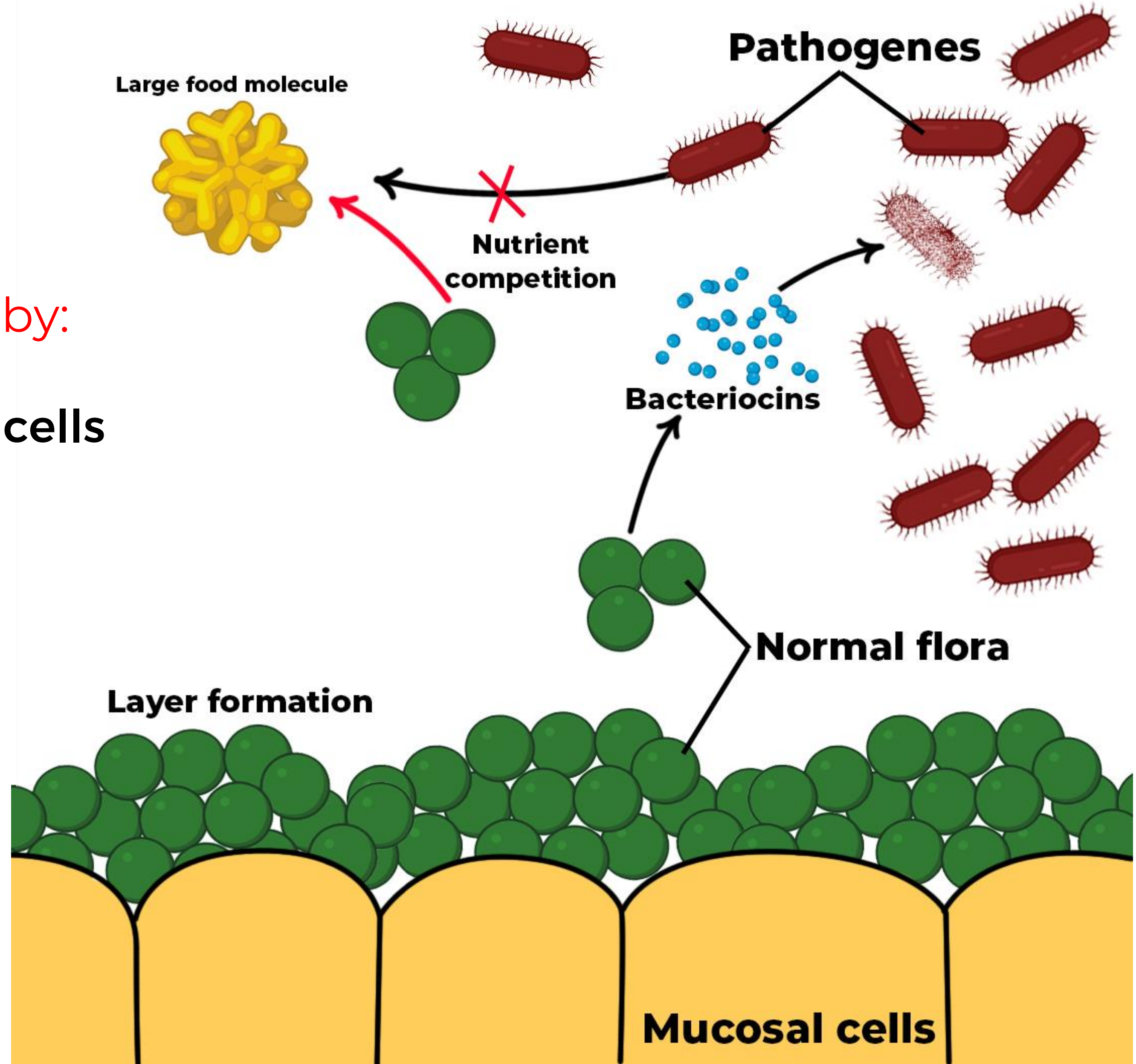
1) Competition for **attachment sites on host cells**

2) Competition for **nutrients**

3) Production of **bacteriocins**

Products that kill other bacteria)

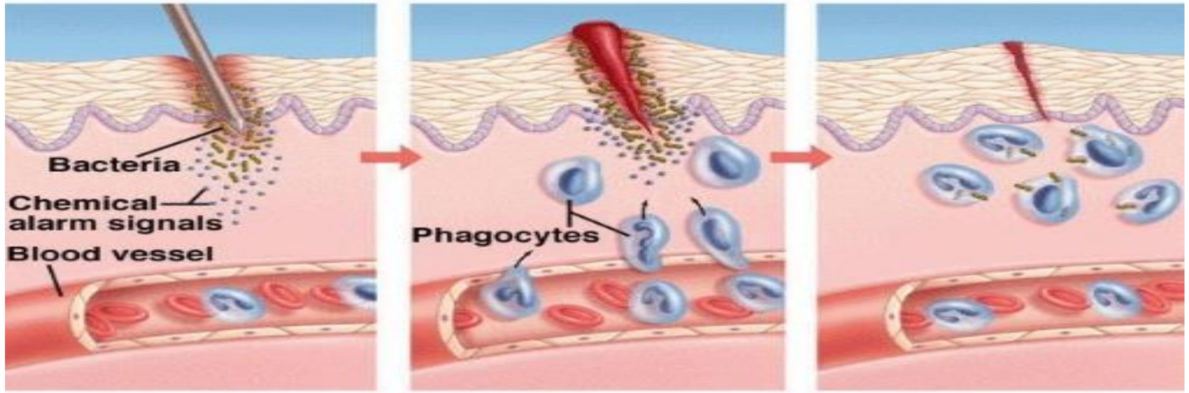
ANB



Inflammatory Response (Inflammation)

Definition

Is a tissue reaction that concentrates circulating WBCs & effector proteins to the site of infection



Mechanism

Vasodilation (VD)

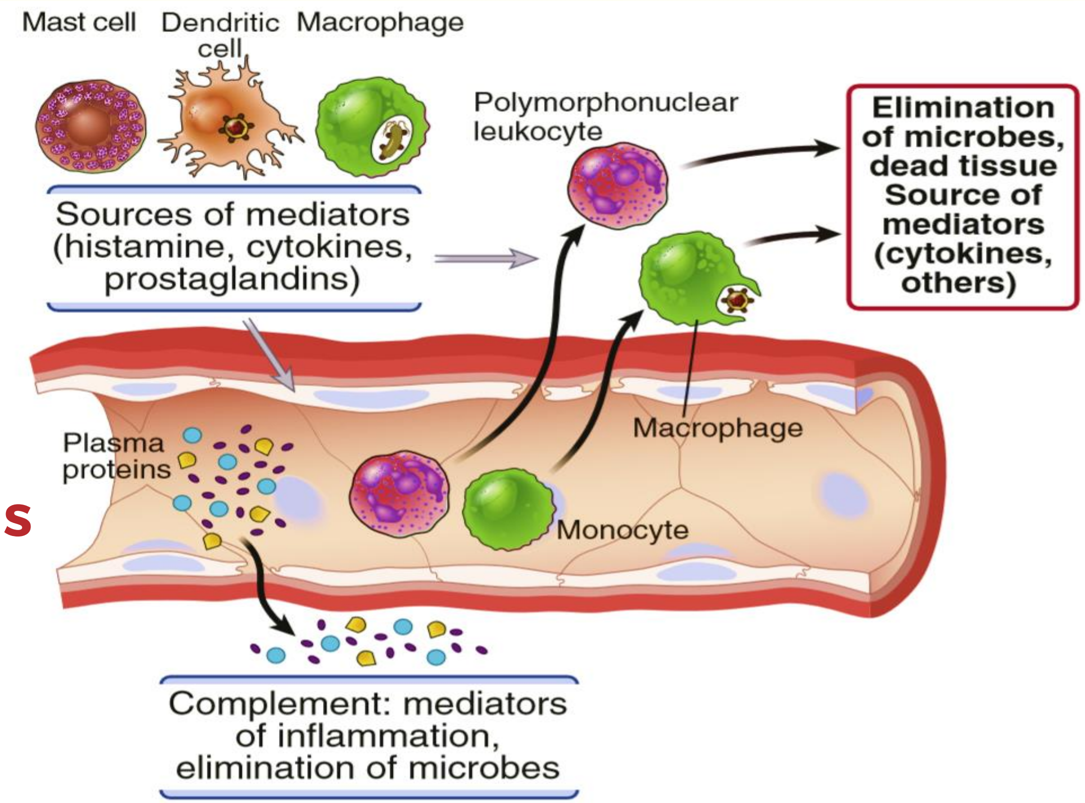
↓

↑ capillary permeability

↓

Migration of WBCs & leakage of effector proteins

from capillaries into infected tissues


Mast cell
Dendritic cell
Macrophage
Sources of mediators (histamine, cytokines, prostaglandins)
Polymorphonuclear leukocyte
Elimination of microbes, dead tissue Source of mediators (cytokines, others)
Macrophage
Plasma proteins
Monocyte
Complement: mediators of inflammation, elimination of microbes

III) Phagocytes & Phagocytosis

A) Neutrophils

B) Monocytes & MQ

C) Dendritic cells

A) Neutrophils

➲ Site & Circulation

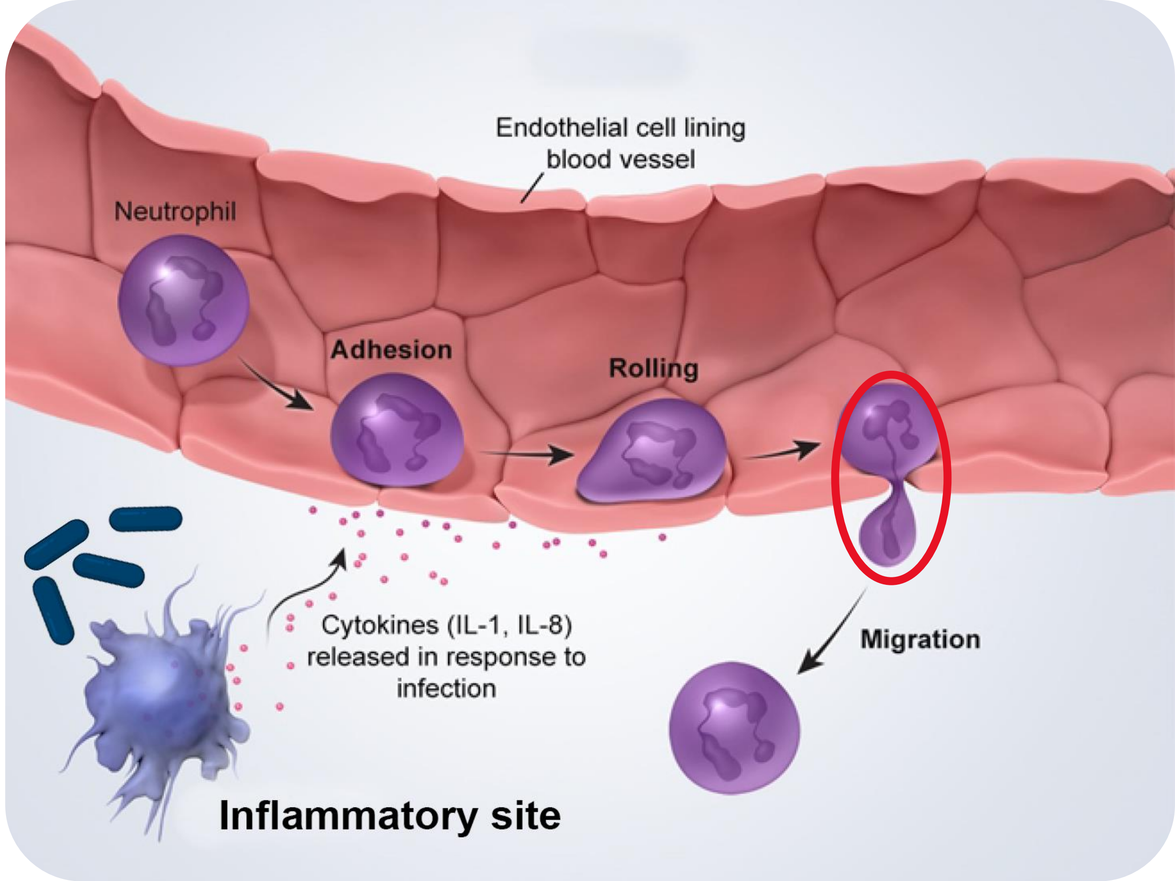
- Most abundant WBCs in blood

↓

1st phagocytic cells that encounter infection in blood

- Recruited (migrate) from blood into tissues (during inflammation)

- ↑ ↑ number in blood in bacterial or fungal infections


Endothelial cell lining blood vessel
Neutrophil
Adhesion
Rolling
Cytokines (IL-1, IL-8) released in response to infection
Migration
Inflammatory site

A) Neutrophils

➲ Granules

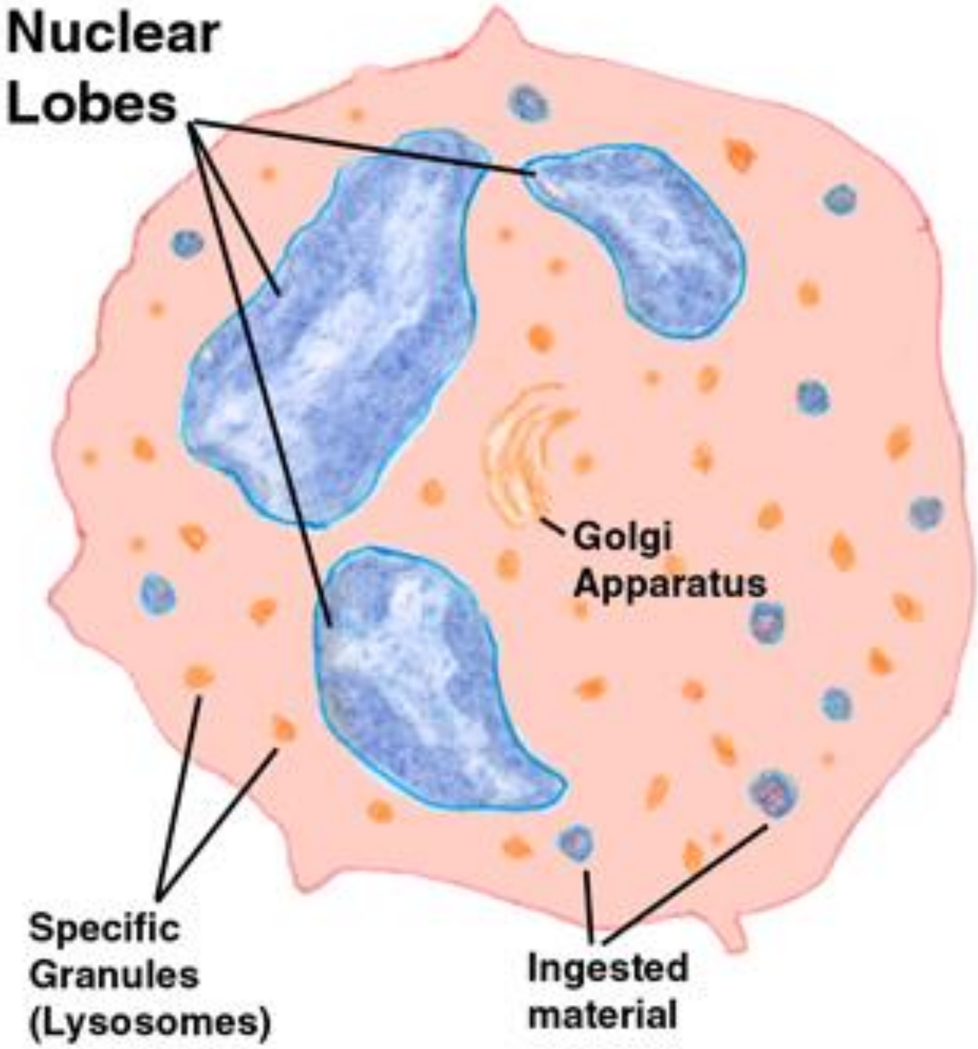
Lysosomes: contain microbicidal substances

E.g. - Lysosymes, Defensins (LD)

- Elastases, proteases

➲ Functions

Phagocytosis



B) Monocytes & MQ

Site & Circulation

Monocytes circulate in **blood**

↓

Maturate into

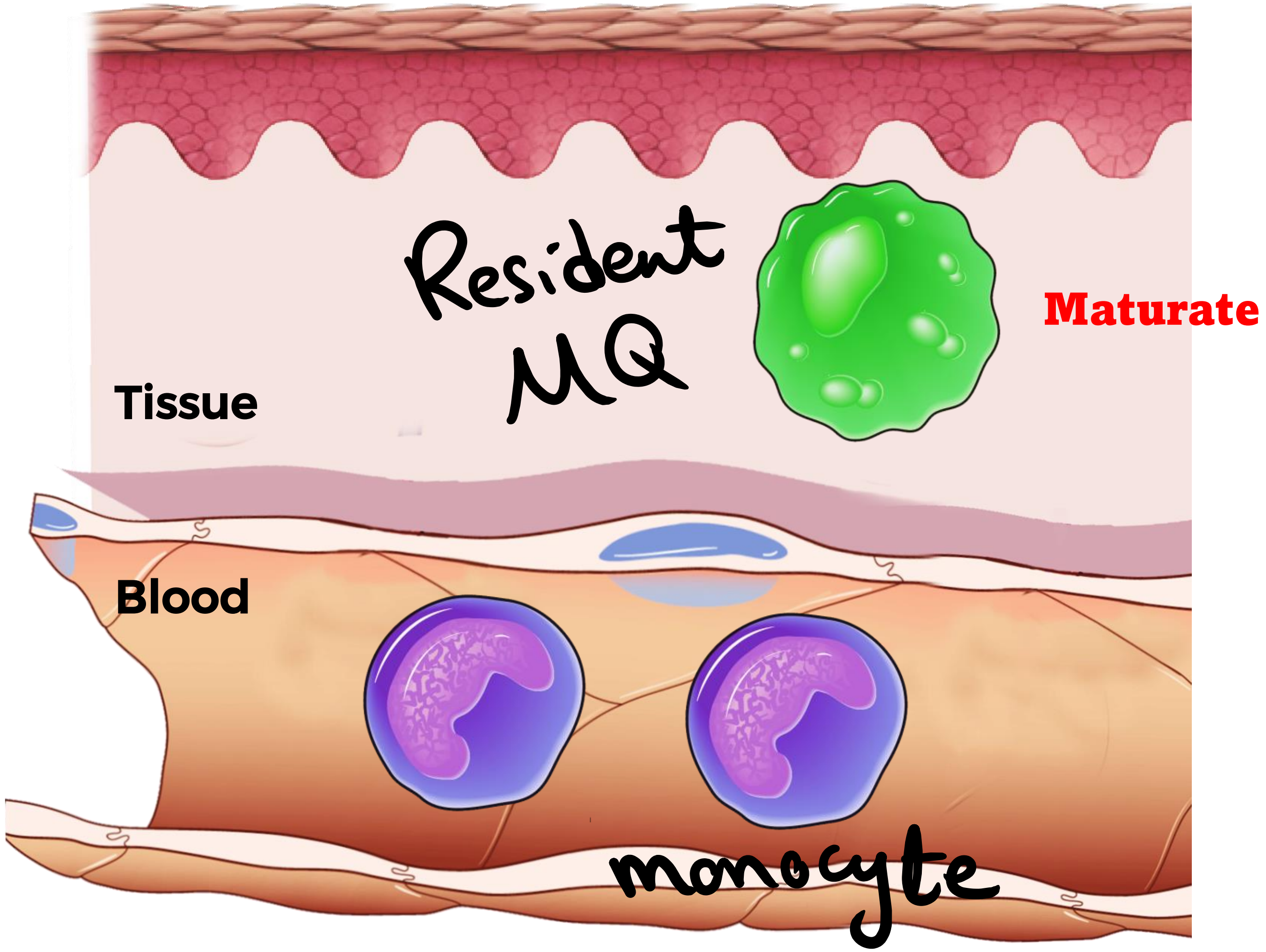
resident macrophages (MQ)

in tissues

Granules

Lysosomes

Functions



1) **Phagocytosis**
2) **Production of inflammatory cytokines**
3) **Antigen presenting cell (APC)** → Activates T cell

C) Dendritic cells

➲ Site & Circulation

1) Skin

2) RT & GIT mucosa

❖ **Migratory cells** : travel to lymph nodes& spleen

↓

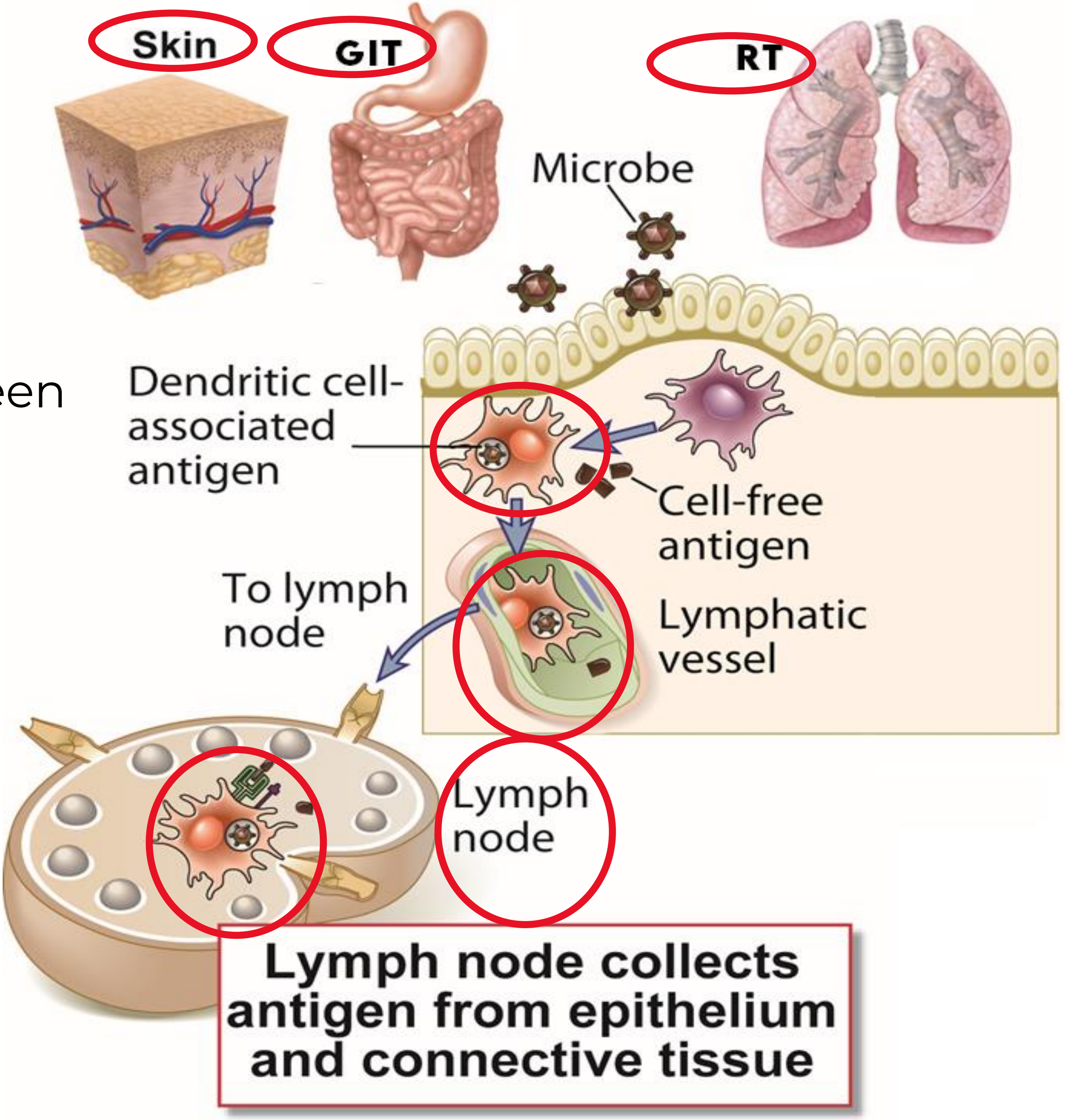
Activate T lymphocytes

(main Ag presenting cell)

➲ Granules

➲ Functions

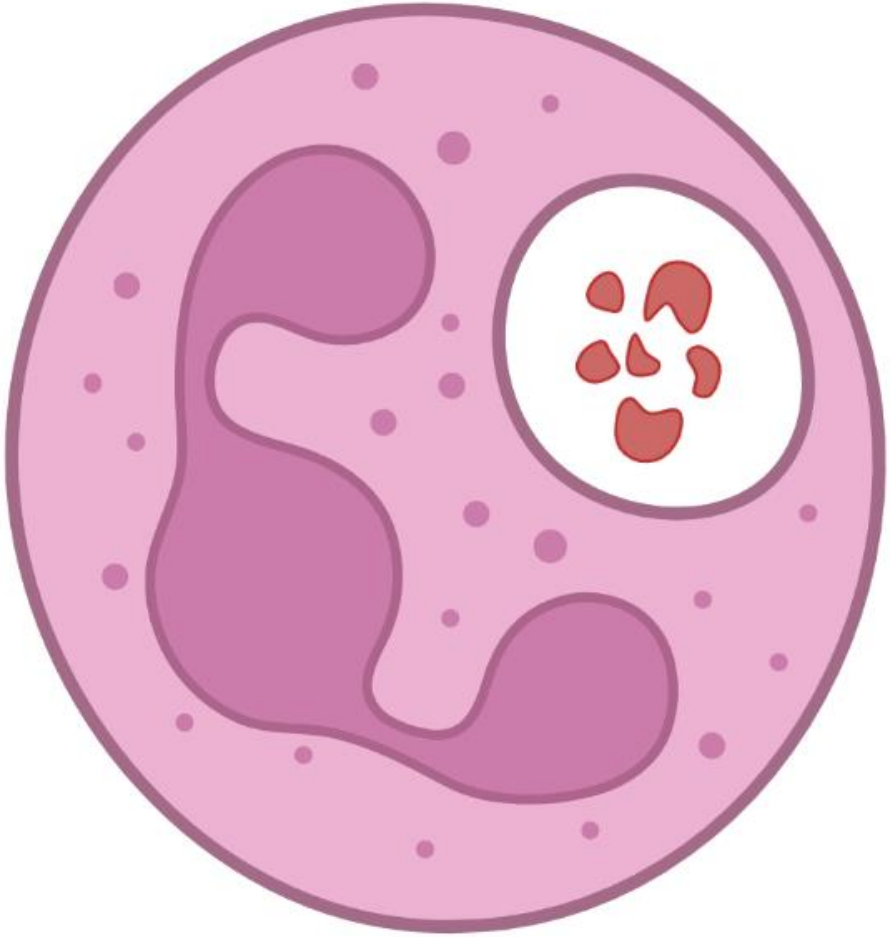
} As macrophage



Lymph node collects antigen from epithelium and connective tissue

Steps of phagocytosis

- A Recognition of microbes
- B Uptake
- A Intracellular killing



Recognition of microbes

By **Pattern recognition receptors (PRRs)**

e.g **Toll like receptors (TLRs)**

- **Functions of PRRs:** **Recognize**

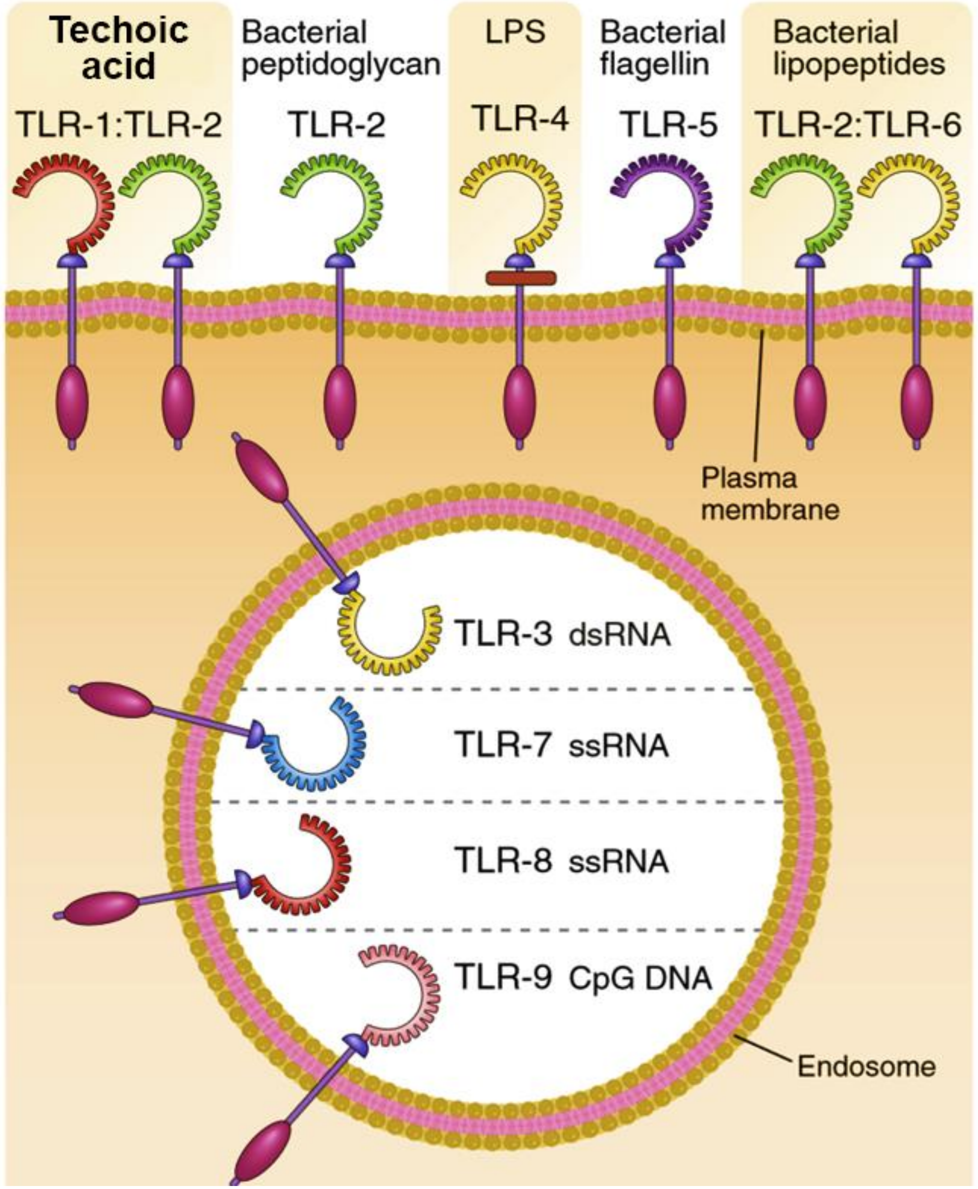
pathogen associated molecular patterns (PAMPs):

Characteristic structures of microbes

(not present in mammalian cells) e.g

1) Bacterial: • Lipopolysaccharides (LPS)
• Techoic acid

2) Viral : nucleic acid



Uptake

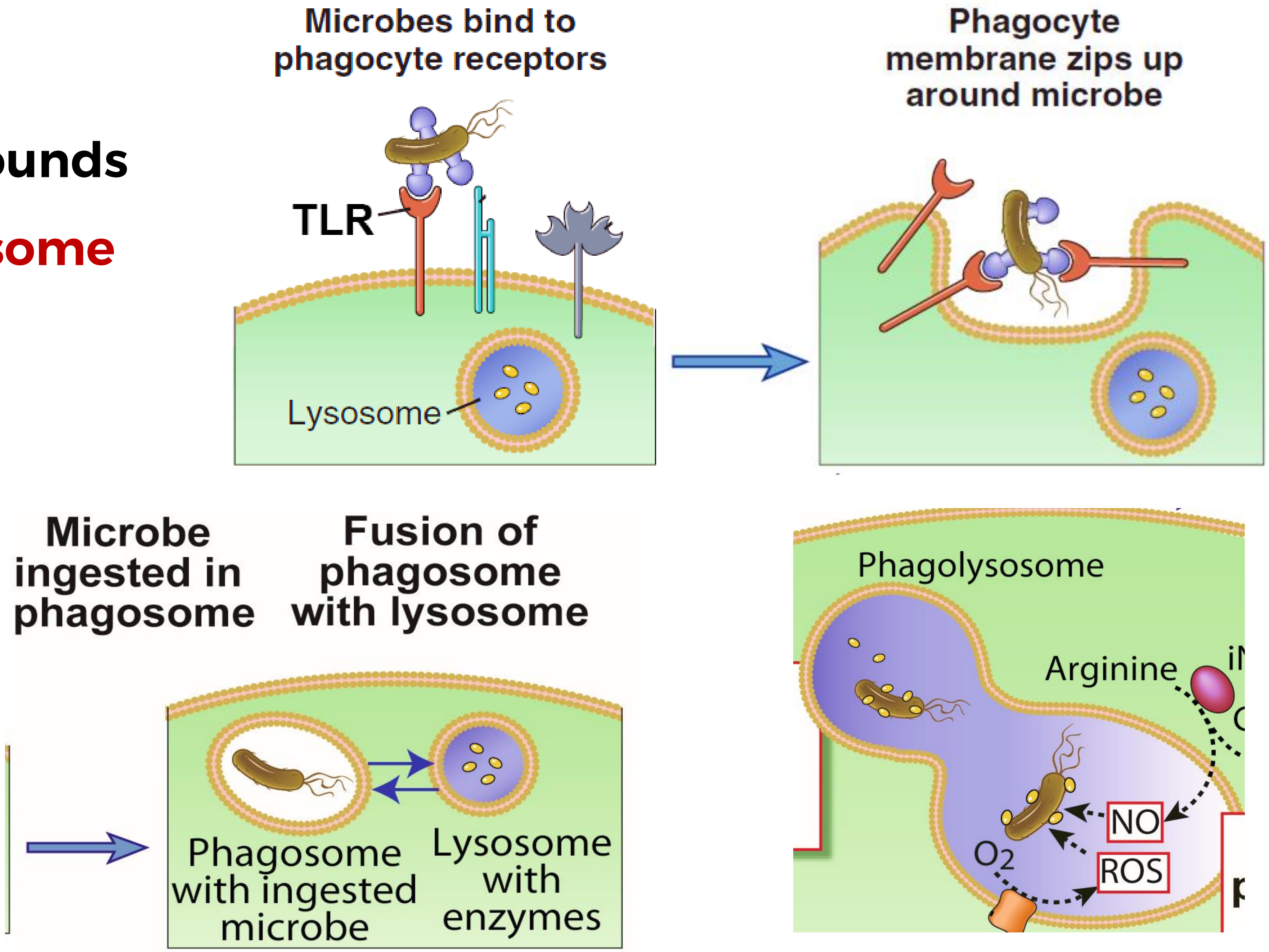
Phagocyte **cell membrane surrounds the organism** forming a **phagosome**

↓

Fuses with lysosome

↓

Phagolysosome


Microbes bind to phagocyte receptors
TLR
Lysosome
Phagocyte membrane zips up around microbe
Microbe ingested in phagosome
Fusion of phagosome with lysosome
Phagosome with ingested microbe
Lysosome with enzymes
Phagolysosome
Arginine
NO
ROS
O2

Intracellular killing (in phagolysosome)

Oxidative killing (Burst)

Oxidase converts O_2

into reactive O_2 species (ROS): **O_2^- & H_2O_2**

↓

Killing of microbe

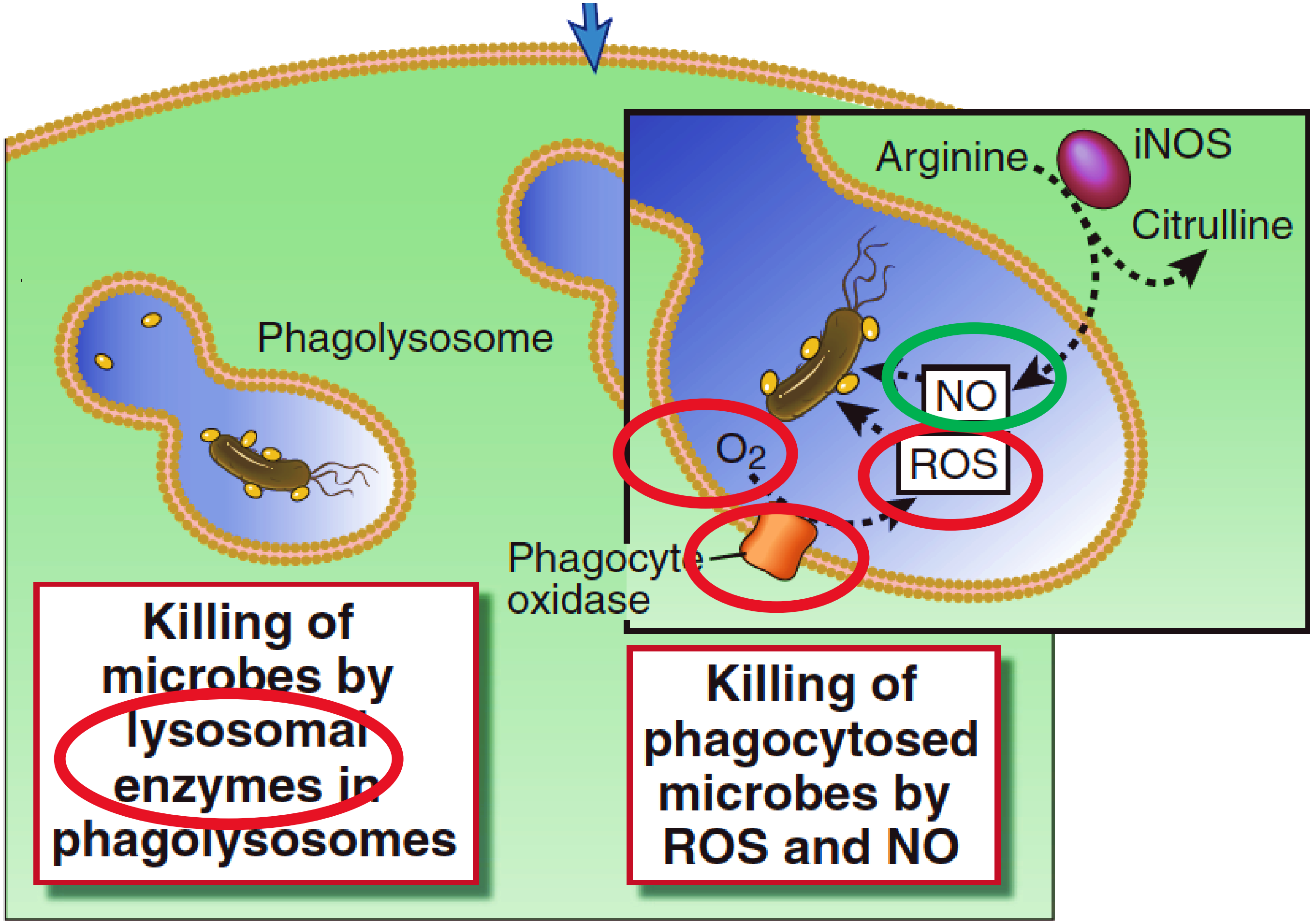
Non oxidative Killing

By **proteolytic enzymes**

in phgolysosomes e.g **elastase**

↓

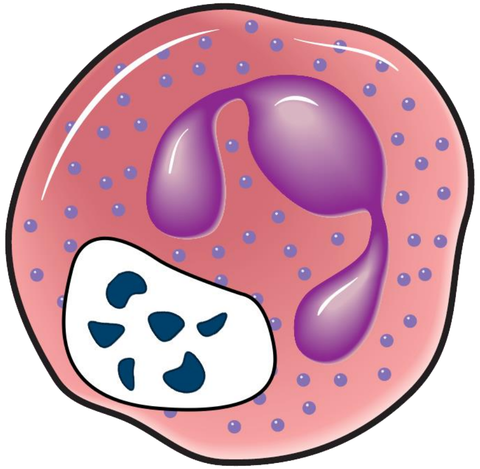
Destruction of microbes

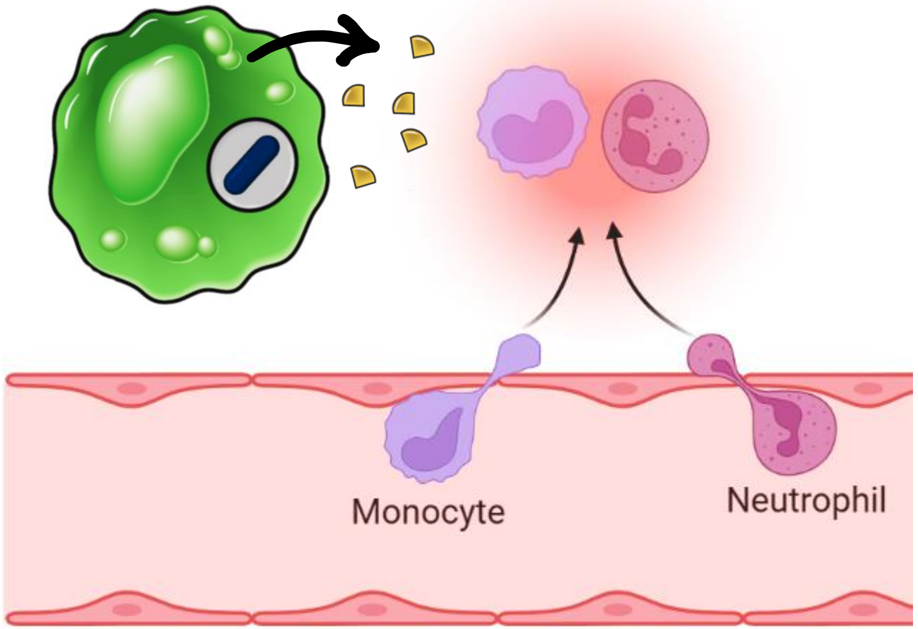

Phagolysosome
Arginine
iNOS
Citrulline
NO
O_2
ROS
Phagocyte oxidase
Killing of microbes by lysosomal enzymes in phagolysosomes
Killing of phagocytosed microbes by ROS and NO

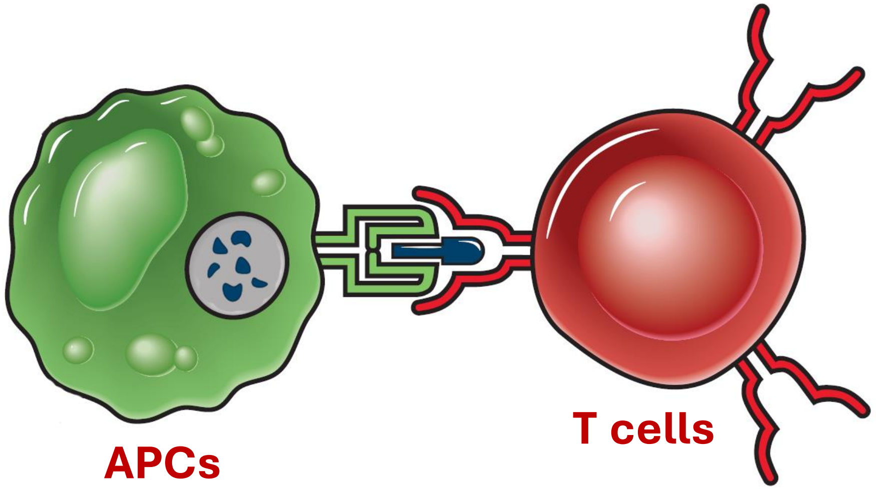
III) Phagocytes & Phagocytosis

Outcome of phagocytosis

Neutrophils	Dendritic cells & Macrophages	
Destroy microbes completely	**Production of inflammatory cytokines** ↓ **Inflammation**	**Present Ag to T cells (APCs)** ↓ **Initiation of adaptive immunity**







Quiz 2

What is the main Ag presenting cells?

A. Neutrophils

B. Eosinophils

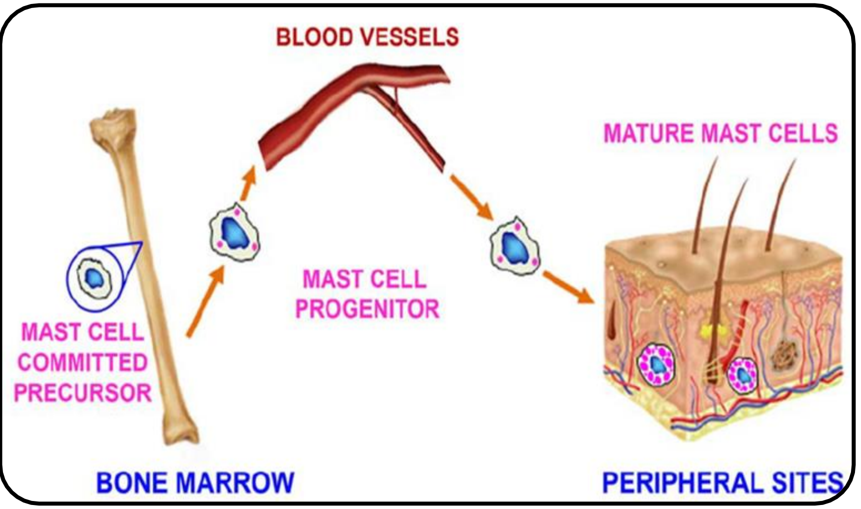
C. Monocytes

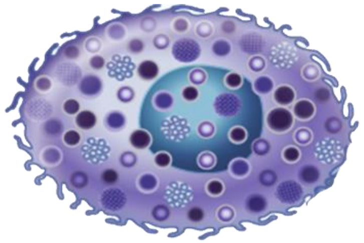
D. Macrophages

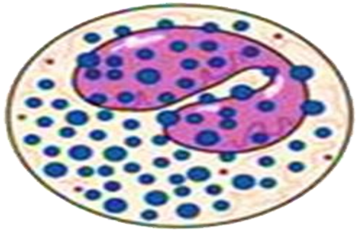
E. Dendritic

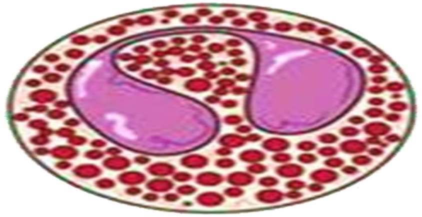
IV) Inflammatory cells involved in allergy

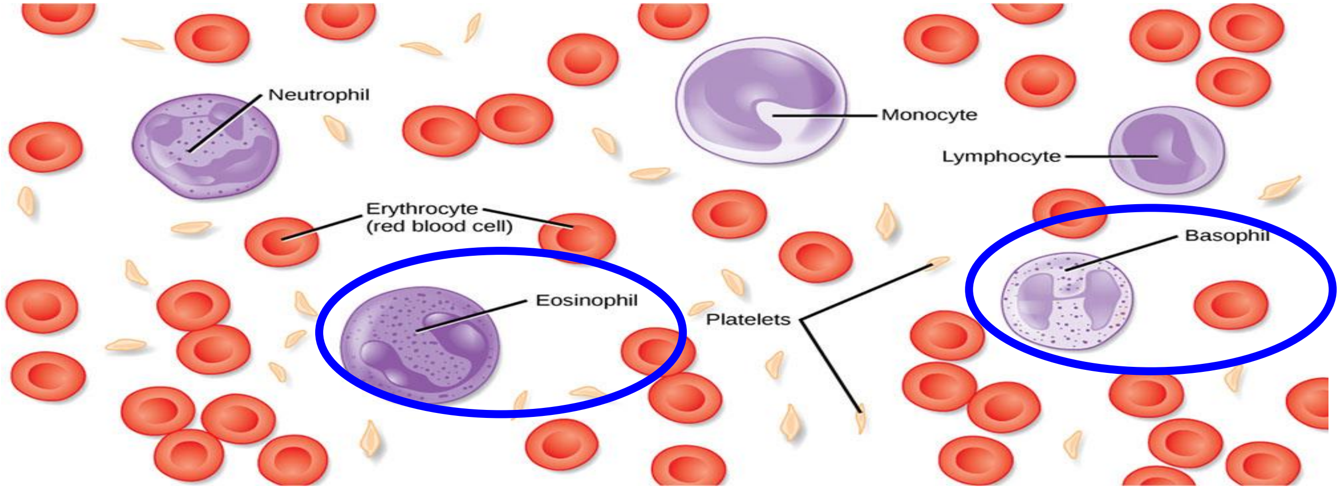
<table>
<tr><th></th><th>Mast cells</th><th>Basophils</th><th>Eosinophils</th></tr>
<tr><td>Site</td><td>Fixed in tissues :
skin, GIT & RT mucosa</td><td colspan="2">In blood → Recruited (migrate) into tissues (during inflammation)</td></tr>
<tr><td>Granules</td><td colspan="2">Contain Histamine (induces vasodilation), cytokines</td><td>Contain cytokines & toxic protein</td></tr>
</table>



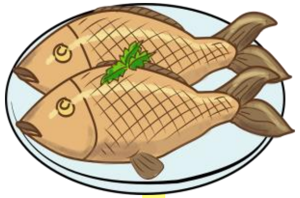
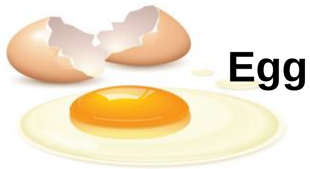


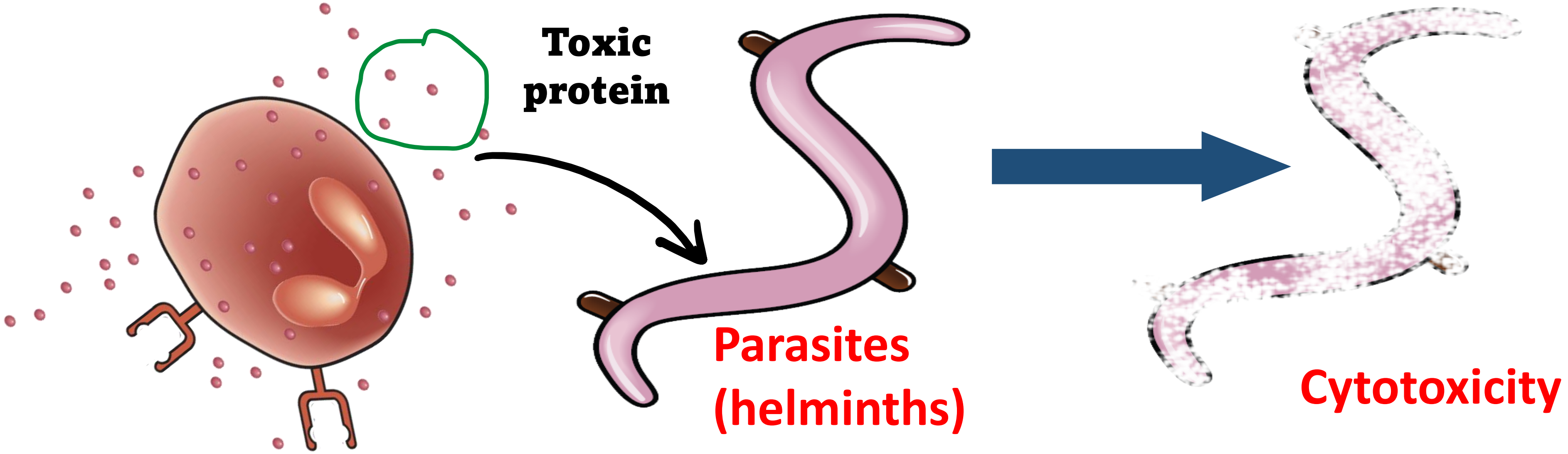






IV) Inflammatory cells involved in allergy

<table>
<tr><th></th><th>Mast cells</th><th>Basophils</th><th>Eosinophils</th></tr>
<tr><td rowspan="2">Role in immunity</td><td colspan="3">1) Inflammation in mucosa
2) Have a role in hypersensitivity (allergy)


Egg</td></tr>
<tr><td colspan="2"></td><td>3) Cytotoxicity (EC killing) of helminths(parasites):
by toxic protein
• ↑ number in blood in parasitic infections</td></tr>
</table>



- ↑ number of **neutrophils** in blood in

bacterial & fungal infections

- ↑ number of **eosinophils** in blood in

parasitic (helminthic) infections

- ↑ number of **lymphocytes** in blood in

Viral infections